

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark
Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 11 December 1996 (11.12.96)	Applicant's or agent's file reference FP41 90211
International application No. PCT/US96/05465	Priority date (day/month/year) 25 April 1995 (25.04.95)
International filing date (day/month/year) 18 April 1996 (18.04.96)	
Applicant EVANS, Ronald, M. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

25 November 1996 (25.11.96)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Catherine Massetti
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 730.91.11

PATENT COOPERATION TREATY

PCT

COMMUNICATION OF
INTERNATIONAL APPLICATIONS

(PCT Article 20)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark
Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ETATS-UNIS D'AMERIQUE

Date of mailing:

30 January 1997 (30.01.97)

in its capacity as designated Office

The International Bureau transmits herewith copies of the international applications having the following international application numbers and international publication numbers:

International application no.:

PCT/US96/05465

International publication no.:

WO96/33724

**CORRECTED VERSION
VERSION CORRIGEE**The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer:

J. Zahra

Telephone No.: (41-22) 730.91.11

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

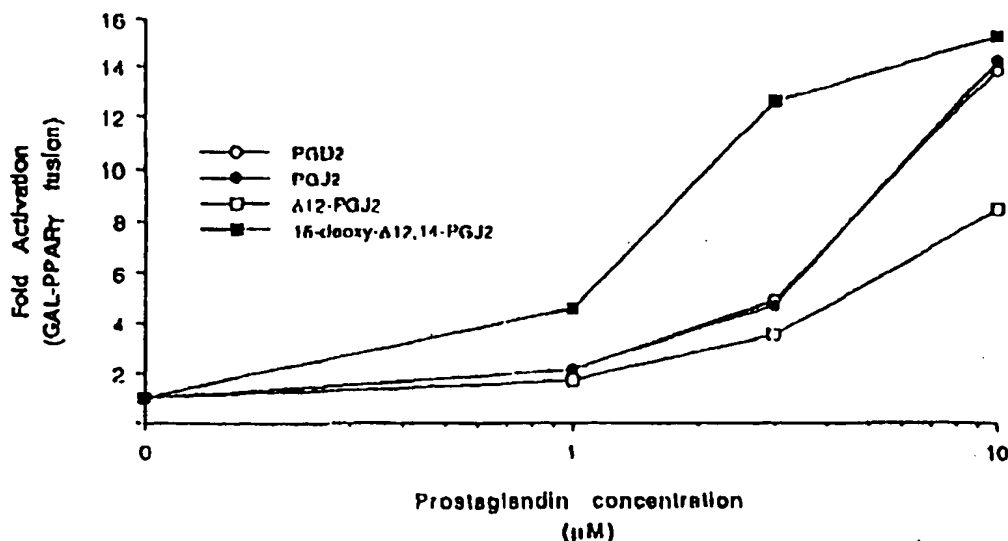


INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification: A61K 31/557		(11) International Publication Number: WO 96/33724
A2		(43) International Publication Date: 31 October 1996 (31.10.96)
(21) International Application Number: PCT/US96/05465		(74) Agent: REITER, Stephen, E.; Pretty, Schroeder, Brueggemann & Clark, Suite 2000, 444 South Flower Street, Los Angeles, CA 90071 (US).
(22) International Filing Date: 18 April 1996 (18.04.96)		(81) Designated States: AU, CA, JP, US, European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).
(30) Priority Data: 08/428,559 25 April 1995 (25.04.95) US 08/465,375 5 June 1995 (05.06.95) US		Published <i>Without international search report and to be republished upon receipt of that report.</i>
(60) Parent Applications or Grants (63) Related by Continuation US 08/428,559 (CIP) Filed on 25 April 1995 (25.04.95) US 08/465,375 (CIP) Filed on 5 June 1995 (05.06.95)		
(71) Applicant (for all designated States except US): THE SALK INSTITUTE FOR BIOLOGICAL STUDIES [US/US]; 10010 North Torrey Pines Road, La Jolla, CA 92037 (US).		
(72) Inventors; and (75) Inventors/Applicants (for US only): EVANS, Ronald, M. [US/US]; 1471 Cottontail Lane, La Jolla, CA 92037 (US). FORMAN, Barry, M. [US/US]; Apartment 299, 8568 Via La Jolla, La Jolla, CA 92037 (US).		

(54) Title: SELECTIVE MODULATORS OF PEROXISOME PROLIFERATOR ACTIVATED RECEPTOR-GAMMA, AND METHODS FOR THE USE THEREOF

Activation of PPAR γ by Prostaglandins



(57) Abstract

In accordance with the present invention, there are provided a class of compounds which are capable of selectively modulating processes mediated by peroxisome proliferator activated receptor-gamma (PPAR- γ). The identification of such compounds makes possible the selective intervention in PPAR- γ mediated pathways, without exerting inadvertent effects on pathways mediated by other PPAR isoforms.

PATENT COOPERATION TREATY

PCT

REC'D 01 JUL 1997



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 69 068 a/fi	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US 96/ 05465	International filing date (day/month/year) 18/04/1996	Priority date (day/month/year) 25/04/1995
International Patent Classification (IPC) or national classification and IPC A61K31/557		
Applicant THE SALK INSTITUTE FOR BIOLOGICAL STUDIES et al.		

- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This **REPORT** consists of a total of 7 sheets, including this cover sheet.
☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
These annexes consists of a total of _____ sheets.

- This report contains indications and corresponding pages relating to the following items:
 - I ☒ Basis of the report
 - II ☐ Priority
 - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☒ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application

Date of submission of the demand 25/11/1996	Date of completion of this report 27.06.97
Name and mailing address of the IPEA/  European Patent Office D-80298 Munich Tel. (+49-89) 2399-0, Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Authorized officer  I. Obrecht Telephone No. 8471

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

Intern. application No.

PCT/US96/05465

I. Basis of the report

1. This report has been drawn up on the basis of (Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.):

☒ the international application as originally filed.

☐ the description, pages _____, as originally filed,
pages _____, filed with the demand,
pages _____, filed with the letter of _____,
pages _____, filed with the letter of _____.

☐ the claims, Nos. _____, as originally filed,
Nos. _____, as amended under Article 19,
Nos. _____, filed with the demand,
Nos. _____, filed with the letter of _____,
Nos. _____, filed with the letter of _____.

☐ the drawings, sheets/fig _____, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,
sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

☐ the description, pages _____.
☐ the claims, Nos. _____.
☐ the drawings, sheets/fig _____.

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

Intern. application No.

PCT/US96/05465

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application,

☒ claims Nos. 1 - 15 _____

because:

☒ the said international application, or the said claims Nos. 1 - 15 _____ relate to the following subject matter which does not require an international preliminary examination (specify):

Methods for the treatment of the human or animal body by surgery or therapy as well as diagnostic methods practiced on the human or animal body and scientific theories (discoveries) are subject-matter on which an International Preliminary Examining Authority is not required to carry out international preliminary examination.

It appears that the method of claims 1 to 15 relates to a discovery, which discovery consists in that a PPAR-gamma selective prostaglandin or prostaglandin-like compound or precursor thereof is able to modulate process mediated by PPAR-gamma, since the aim of the method is not clear or mentioned.

The method of claims 1 to 15 relates to a method for the treatment of the human or animal body by surgery or therapy, if the method is carried out in the human body.

☒ the description, claims or drawings (indicate particular elements below) or said claims Nos. 1 - 15 _____ are so unclear that no meaningful opinion could be formed (specify):

Claims 1 to 15 relate to a method for modulating process(es) mediated by PPAR-gamma, said method comprising conducting said process(es) in the presence of at least

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

Intern. application No.

PCT/US96/05465

one PPAR-gamma selective prostaglandin or
prostaglandin-like compound or precursor thereof.

It is not clear whether this method is carried out in
vivo or in vitro.

The subject-matter of claims 1 to 15 is not susceptible
of industrial application, since the aim of present
claims 1 to 15 is not apparent from the present wording.

[] the claims, or said claims Nos. _____ are so inadequately supported by
the description that no meaningful opinion could be formed.

[] no international search report has been established for said claims
Nos. _____.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

Intern. application No.

PCT/US96/05465

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 16 - 23 _____	YES
	Claims _____	NO
Inventive Step (IS)	Claims 16 - 23 _____	YES
	Claims _____	NO
Industrial Applicability (IA)	Claims 16 - 21 _____	YES
	Claims 22, 23 (see item 1). below) _____	NO

2. CITATIONS AND EXPLANATIONS

- 1). For the assessment of the present Claims 22 and 23 on the question whether they are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to methods for treatment of the human or animal body by surgery or therapy or the use of a compound in medical treatment, but will allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.
- 2). Document (1) = Proceedings of the national academy of Sciences of USA, vol. 91, July 1994, pages 7355-7359, XP002007699, S.A. Kliewer et Al.: "Differential expression and activation of a family of murine peroxisome proliferator-activated receptors" discloses a physiological role for PPAR α in the regulation of lipid

metabolism (in particular the metabolism of fatty acids). Significant activation of PPAR-gamma was obtained upon treatment with LY-171883. The differential expression of PPAR-gamma in the adrenal suggests that this isoform may respond to an adrenal-enriched ligand. See the whole document.

This document fails to teach or suggest that administering an amount of a peroxisome proliferator activated receptor gamma (PPAR-gamma) antagonist effective to block cell differentiation to produce lipid-accumulating cells administered to a subject would be active for preventing obesity.

The subject-matter of claims 22 and 23 drafted in order to obviate the above comments under item 1)., would be novel over the teaching of document (1) and would involve an inventive step.

- 3). The method of testing a compound for its ability to regulate transcription-activating effects of a PPAR-gamma of claims 16 to 21 is new in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT) and involves an inventive step (Rule 65(1)(2) PCT).

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

Intern. application No.
PCT/US96/05465

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
-------------------------------	--------------------------------------	---------------------------------	---

The current assessment is based on the assumption that all claims enjoy priority rights from the filing date of the priority document. If it later turns out that this is not correct, the documents:

Journal of biological chemistry, vol. 270, no. 22, 2
june 1995, pages 12953-6 XP002007698,

Journal of biological chemistry, vol. 270, no. 41, 13
October 1995, pages 23975-83 XP002008288,

Cell, vol. 83, 1 Dezember 1995, pages 813-19,
XP000575884

Cell, vol. 83, 1 Dezember 1995, pages 803-812,
XP000575803,

cited in the international search report could become
relevant to assess whether claims 1 to 23 satisfy the
criteria set forth in Article 33(1) PCT.

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure (day/month/year)	Date of written disclosure referring to non-written disclosure (day/month/year)
--------------------------------	--	---

PCT

09/155252

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference FP41 90211	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 96/ 05465	International filing date (day/month/year) 18/04/1996	(Earliest) Priority Date (day/month/year) 25/04/1995
Applicant THE SALK INSTITUTE FOR BIOLOGICAL STUDIES et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☒ Certain claims were found unsearchable (see Box I).

2. ☐ Unity of invention is lacking (see Box II).

3. ☐ The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the international search was carried out on the basis of the sequence listing

☐ filed with the international application.

☒ furnished by the applicant separately from the international application,

☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.

☐ Transcribed by this Authority

4. With regard to the title, ☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is:

Figure No. 1,2 ☐ as suggested by the applicant.

☐ None of the figures.

☒ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 96/ 05465

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 1-15, 22 and 23 are directed to a method of treatment of (diagnostic method practised on) the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K31/557

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 91, July 1994, WASHINGTON US, pages 7355-7359, XP002007699 S.A. KLIEWER ET AL.: "Differential expression and activation of a family of murine peroxisome proliferator-activated receptors" see the whole document ---	22,23
A	GENE EXPRESSION, vol. 4, 1995, pages 281-299, XP000057446 M.E. GREENE ET AL.: "Isolation of the human peroxisome proliferator activated receptor gamma cDNA" --- -/--	1-23

☒ Further documents are listed in the continuation of box C.

☐ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

12. December 1996

Date of mailing of the international search report

13-12-1996

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentaan 2
NL - 2280 HV Rijswijk
Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl,
Fax (+ 31-70) 340-3016

Authorized officer

De Jong, B

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 96/05465

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

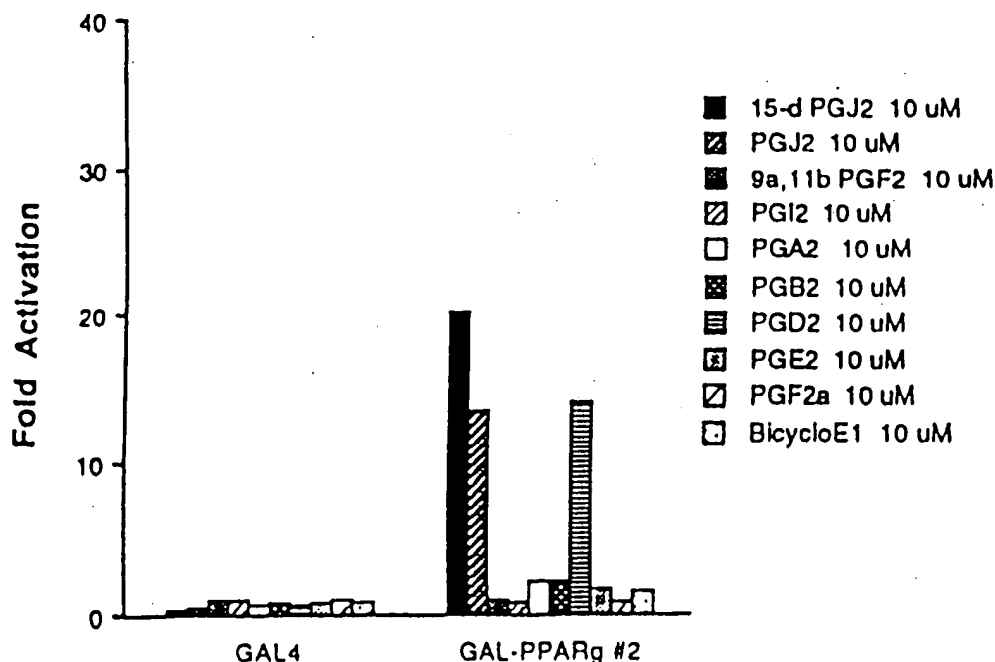
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 270, no. 22, 2 June 1995, MD US, pages 12953-12956, XP002007698 J.M.LEHMANN ET AL.: "An antidiabetic thiazolidinone is a high affinity ligand for peroxisome proliferator-activated receptor" see the whole document ---	22,23
P,X	J. BIOL. CHEM., vol. 270, no. 41, 13 October 1995, pages 23975-23983, XP002008288 K. YU ET AL.: "Differential activation of peroxisome proliferator-activated receptors by eicosanoids" see the whole document ---	1-23
P,X	CELL, vol. 83, 1 December 1995, pages 813-819, XP000575884 S.A. KLIEWER ET AL.: "A prostaglandin J2 metabolite binds peroxisome proliferator-activated receptor gamma and promotes adipocyte differentiation" see the whole document ---	1-23
P,X	CELL, vol. 83, 1 December 1995, pages 803-812, XP000575803 B.M. FORMAN ET AL.: "15-DEOXY-DELTA12,14-PROSTAGLANDIN J2 IS A LIGAND FOR THE ADIPOCYTE DETERMINATION FACTOR PPAR GAMMA" see the whole document -----	1-23



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : A61K 31/557		A3	(11) International Publication Number: WO 96/33724
			(43) International Publication Date: 31 October 1996 (31.10.96)
(21) International Application Number: PCT/US96/05465		(74) Agent: REITER, Stephen, E.; Pretty, Schroeder, Brueggemann & Clark, Suite 2000, 444 South Flower Street, Los Angeles, CA 90071 (US).	
(22) International Filing Date: 18 April 1996 (18.04.96)			
(30) Priority Data: 08/428,559 25 April 1995 (25.04.95) US 08/465,375 5 June 1995 (05.06.95) US		(81) Designated States: AU, CA, JP, US, European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).	
(60) Parent Applications or Grants (63) Related by Continuation US 08/428,559 (CIP) Filed on 25 April 1995 (25.04.95) US 08/465,375 (CIP) Filed on 5 June 1995 (05.06.95)		Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>	
(71) Applicant (for all designated States except US): THE SALK INSTITUTE FOR BIOLOGICAL STUDIES [US/US]; 10010 North Torrey Pines Road, La Jolla, CA 92037 (US).		(88) Date of publication of the international search report: 30 January 1997 (30.01.97)	
(72) Inventors; and (75) Inventors/Applicants (for US only): EVANS, Ronald, M. [US/US]; 1471 Cottontail Lane, La Jolla, CA 92037 (US). FORMAN, Barry, M. [US/US]; Apartment 299, 8568 Via La Jolla, La Jolla, CA 92037 (US).			

(54) Title: SELECTIVE MODULATORS OF PEROXISOME PROLIFERATOR ACTIVATED RECEPTOR-GAMMA, AND METHODS FOR THE USE THEREOF



(57) Abstract

In accordance with the present invention, there are provided a class of compounds which are capable of selectively modulating processes mediated by peroxisome proliferator activated receptor-gamma (PPAR- γ). The identification of such compounds makes possible the selective intervention in PPAR- γ mediated pathways, without exerting inadvertent effects on pathways mediated by other PPAR isoforms.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AM	Armenia	GB	United Kingdom	MW	Malawi
AT	Austria	GE	Georgia	MX	Mexico
AU	Australia	GN	Guinea	NE	Niger
BB	Barbados	GR	Greece	NL	Netherlands
BE	Belgium	HU	Hungary	NO	Norway
BF	Burkina Faso	IE	Ireland	NZ	New Zealand
BG	Bulgaria	IT	Italy	PL	Poland
BJ	Benin	JP	Japan	PT	Portugal
BR	Brazil	KE	Kenya	RO	Romania
BY	Belarus	KG	Kyrgyzstan	RU	Russian Federation
CA	Canada	KP	Democratic People's Republic of Korea	SD	Sudan
CF	Central African Republic	KR	Republic of Korea	SE	Sweden
CG	Congo	KZ	Kazakhstan	SG	Singapore
CH	Switzerland	LI	Liechtenstein	SI	Slovenia
CI	Côte d'Ivoire	LK	Sri Lanka	SK	Slovakia
CM	Cameroon	LR	Liberia	SN	Senegal
CN	China	LT	Lithuania	SZ	Swaziland
CS	Czechoslovakia	LU	Luxembourg	TD	Chad
CZ	Czech Republic	LV	Latvia	TG	Togo
DE	Germany	MC	Monaco	TJ	Tajikistan
DK	Denmark	MD	Republic of Moldova	TT	Trinidad and Tobago
EE	Estonia	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	UG	Uganda
FI	Finland	MN	Mongolia	US	United States of America
FR	France	MR	Mauritania	UZ	Uzbekistan
GA	Gabon			VN	Viet Nam

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 96/05465

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 270, no. 22, 2 June 1995, MD US, pages 12953-12956, XP002007698 J.M.LEHMANN ET AL.: "An antidiabetic thiazolidinone is a high affinity ligand for peroxisome proliferator-activated receptor" see the whole document ---	22,23
P,X	J. BIOL. CHEM., vol. 270, no. 41, 13 October 1995, pages 23975-23983, XP002008288 K. YU ET AL.: "Differential activation of peroxisome proliferator-activated receptors by eicosanoids" see the whole document ---	1-23
P,X	CELL, vol. 83, 1 December 1995, pages 813-819, XP000575884 S.A. KLIEWER ET AL.: "A prostaglandin J2 metabolite binds peroxisome proliferator-activated receptor gamma and promotes adipocyte differentiation" see the whole document ---	1-23
P,X	CELL, vol. 83, 1 December 1995, pages 803-812, XP000575803 B.M. FORMAN ET AL.: "15-DEOXY-DELTA12,14-PROSTAGLANDIN J2 IS A LIGAND FOR THE ADIPOCYTE DETERMINATION FACTOR PPAR GAMMA" see the whole document -----	1-23

A. CLASSIFICATION OF SUBJECT MATTER IPC 6 A61K31/557		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols) IPC 6 A61K		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used)		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 91, July 1994, WASHINGTON US, pages 7355-7359, XP002007699 S.A. KIEWER ET AL.: "Differential expression and activation of a family of murine peroxisome proliferator-activated receptors" see the whole document ---	22,23
A	GENE EXPRESSION, vol. 4, 1995, pages 281-299, XP000057446 M.E. GREENE ET AL.: "Isolation of the human peroxisome proliferator activated receptor gamma cDNA" --- <div style="text-align: center;">-/--</div>	1-23
<div style="display: flex; justify-content: space-between;"> <input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input type="checkbox"/> Patent family members are listed in annex. </div>		
* Special categories of cited documents :		
<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p>*A* document defining the general state of the art which is not considered to be of particular relevance</p> <p>*E* earlier document but published on or after the international filing date</p> <p>*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>*O* document referring to an oral disclosure, use, exhibition or other means</p> <p>*P* document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 45%;"> <p>*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</p> <p>*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>* & * document member of the same patent family</p> </div> </div>		
Date of the actual completion of the international search	Date of mailing of the international search report	
12. December 1996	18.12.96	
Name and mailing address of the ISA	Authorized officer	
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+ 31-70) 340-3016	De Jong, B	

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 96/05465

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 1-15, 22 and 23 are directed to a method of treatment of (diagnostic method practised on) the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.